HIGH DENSITY GROWTH OF T7 EXPRESSION STRAINS
WITH AUTO-INDUCTION OPTION

Abstract of the Disclosure

[0050] Disclosed is a method for promoting auto-induction of transcription of cloned DNA in cultures of bacterial cells grown batchwise, the transcription being under the control of a promoter whose activity can be induced by an exogenous inducer whose ability to induce said promoter is dependent on the metabolic state of said bacterial cells. Initially, a culture media is provided which includes: i) an inducer that causes induction of transcription from said promoter in said bacterial cells; and ii) a metabolite that prevents induction by said inducer, the concentration of said metabolite being adjusted so as to substantially preclude induction by said inducer in the early stages of growth of the bacterial culture, but such that said metabolite is depleted to a level that allows induction by said inducer at a later stage of growth. The culture medium is inoculated with a bacterial inoculum, the inoculum comprising bacterial cells containing cloned DNA, the transcription of which is induced by said inducer. The culture is then incubated under conditions appropriate for growth of the bacterial cells. Also disclosed is a method for improving the production of a selenomethionine-containing protein or polypeptide in a bacterial cell, the protein or polypeptide being produced by recombinant DNA techniques, the bacterial cell encoding a vitamin B12-dependent homocysteine methylase. The method for improving the production of this protein or polypeptide includes culturing the bacterial cell in a culture medium containing vitamin B12. Finally, disclosed is a method for suppressing transcription of cloned DNA in cultures of bacterial cells grown batchwise, said transcription being under the control of a promoter whose activity can be induced by an exogenous inducer whose ability to induce said promoter is dependent on the metabolic state of said bacterial cells. This aspect includes the steps of: a) providing a culture medium comprising a carbon source whose uptake and metabolism by said bacterial cells suppresses induction of transcription from said promoter; b) inoculating the culture medium with a bacterial

inoculum, the inoculum comprising bacterial cells containing cloned DNA, the transcription of which is suppressed by the carbon source; and c) incubating the culture of step b), with shaking, under conditions appropriate for growth of the bacterial cells.